

AMENDMENT TO THE CLAIMS

Please cancel claims 1-18.

Please amend claims 19, 20, 22, 24, 25, 36 and 38.

Please add claims 39 and 40.

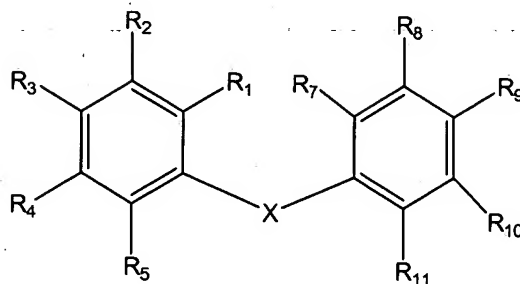
This listing will replace all prior versions, and listings, of claims in this application.

Listing of Claims:

Claims 1-18 (canceled).

Claim 19 (currently amended): A composition comprising:

a) a compound of the formula:



wherein:

X is selected from  $-\text{C}(\text{O})-\text{N}(\text{R}_6)-$ ,  $-\text{N}(\text{R}_6)-\text{C}(\text{O})-$ ,  $-\text{CH}_2-\text{N}(\text{R}_6)-$ ,  $-\text{N}(\text{R}_6)-\text{CH}_2-$ ,  $-\text{N}(\text{R}_6)-\text{S}(\text{O})_2-$ ,  $-\text{S}(\text{O})_2-\text{N}(\text{R}_6)-$ ,  $-\text{C}(\text{R}_{12})(\text{R}_{12})-\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})-\text{C}(\text{R}_{12})(\text{R}_{12})-$ ,  $-\text{C}(\text{R}_{12})(\text{R}_{12})-\text{S}(\text{O})_2-$ ,  $-\text{S}(\text{O})_2-\text{C}(\text{R}_{12})(\text{R}_{12})-$ ,  $-\text{S}(\text{O})_2-\text{O}-$ ,  $-\text{O}-\text{S}(\text{O})_2-$ ,  $-\text{NR}_6-\text{C}(\text{O})-\text{Y}-$  or  $\text{Y}-\text{C}(\text{O})-\text{NR}_6-$ ; wherein

each  $\text{R}_6$  is independently selected from hydrogen,  $\text{C}_1$ - $\text{C}_4$  straight or branched alkyl,  $\text{C}_2$ - $\text{C}_4$  straight or branched alkenyl or alkynyl, Ar-substituted- $\text{C}_1$ - $\text{C}_4$  straight or branched alkyl, or Ar-substituted- $\text{C}_2$ - $\text{C}_4$  straight or branched alkenyl or alkynyl; wherein

$\text{R}_6$  is optionally substituted with up to 3 substituents independently selected from halo, hydroxy, nitro, cyano or amino;

each  $\text{R}_{12}$  is independently selected from  $\text{R}_6$ ,  $\text{W}-[\text{C}_1$ - $\text{C}_4$  straight or branched alkyl],  $\text{W}-[\text{C}_2$ - $\text{C}_4$  straight or branched alkenyl or alkynyl], Ar-substituted- $[\text{W}-[\text{C}_1$ - $\text{C}_4$  straight or branched alkyl]]], Ar-substituted- $[\text{W}-[\text{C}_2$ - $\text{C}_4$  straight or branched alkenyl or alkynyl]]], O-Ar,  $\text{N}(\text{R}_6)$ -Ar, S-Ar,  $\text{S}(\text{O})$ -Ar,  $\text{S}(\text{O})_2$ -Ar,  $\text{S}-\text{C}(\text{O})\text{H}$ ,  $\text{N}(\text{R}_6)-\text{C}(\text{O})\text{H}$ , or  $\text{O}-\text{C}(\text{O})\text{H}$ ; wherein

W is O-, O-C(O)-, S-, S(O)-, S(O)<sub>2</sub>-, S-C(O)-, N(R<sub>6</sub>)-, or N(R<sub>6</sub>)-C(O)-; and wherein each R<sub>12</sub> is optionally and independently substituted with up to 3 substituents independently selected from halo, hydroxy, nitro, cyano or amino;

Y is selected from -O-, -S-, -C≡C-, -C(R<sub>12</sub>)<sub>2</sub>-C(R<sub>12</sub>)<sub>2</sub>-, -C(R<sub>12</sub>)<sub>2</sub>- or -C(R<sub>12</sub>)=C(R<sub>12</sub>)-;

each of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> is independently selected from hydrogen, halo, hydroxy, cyano, nitro, amino, -C(O)NH<sub>2</sub>, Z-[(C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl], Z-[(C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl], Ar-substituted-[(C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl], Ar-substituted-[(C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl], Ar, Q-Ar, [(C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl]-Q-Ar, [(C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl]-Q-Ar, O-[(C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl]-Q-Ar, O-[(C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl]-Q-Ar, [(C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl]-Q-R<sub>13</sub>, [(C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl]-Q-R<sub>13</sub>, or any two adjacent groups selected from either R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> or R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub> may be taken together with the carbon atoms to which they are bound to form a 5 to 6-membered aromatic carbocyclic or heterocyclic ring; wherein

Z is selected from a bond, O-, S-, S(O)<sub>2</sub>-, C(O)-, OC(O)-, or N(H)C(O)-;

Q is selected from O, -O-C(O)-, -C(O)-O-, -N(H)-C(O)-O-, -O-N(H)-C(O)-, -N(H)-C(O)-, -C(O)-N(H)-, -O-C(O)-N(H)-, or -C(O)-N(H)-O-;

Ar is selected from phenyl, 1-naphthyl, 2-naphthyl, indenyl, azulenyl, fluorenyl, anthracenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, 2-pyrazolyl, pyrazolidinyl, isoxazolyl, isotriazolyl, 1,2,3-oxadiazolyl, 1,2,3-triazolyl, 1,3,4-thiadiazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazinyl, 1,3,5-trithianyl, indoliziny, indolyl, isoindolyl, 3H-indolyl, indolinyl, benzo[b]furanyl, benzo[b]thiophenyl, 1H-indazolyl, benzimidazolyl, benzthiazolyl, purinyl, 4H-quinoliziny, quinoliny, isoquinoliny, 1,2,3,4-tetrahydro-isoquinoliny, cinnoliny, phthalazinyl, quinazolinyl, quinoxaliny, 1,8-naphthyridiny, peridiny, carbazolyl, acridiny, phenazinyl, phenothiazinyl or phenoxazinyl or other chemically feasible monocyclic, bicyclic or tricyclic ring systems, wherein each ring consists of 5 to 7 ring atoms and wherein each ring comprises 0 to 3 heteroatoms independently selected from N, O and S;

R<sub>13</sub> is selected from [C<sub>1</sub>-C<sub>12</sub> straight or branched alkyl] or, [C<sub>2</sub>-C<sub>12</sub> straight or branched alkenyl or alkynyl]; wherein R<sub>13</sub> is optionally substituted with 1 to 4 substituents independently selected from R<sub>14</sub> or R<sub>15</sub>, wherein

each R<sub>14</sub> is a monocyclic or a bicyclic ring system consisting of 3 to 7 members per ring, wherein said ring system optionally comprises up to 4 heteroatoms selected from N, O, and S; wherein a CH<sub>2</sub> adjacent to said N, O or S may be substituted with C(O); and wherein R<sub>14</sub> optionally comprises up to 2 substituents independently selected from (C<sub>1</sub>-C<sub>4</sub>)-straight or

branched alkyl, (C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, (CH<sub>2</sub>)<sub>n</sub>-R<sub>16</sub>, -S-(CH<sub>2</sub>)<sub>n</sub>-R<sub>16</sub>, -S(O)-(CH<sub>2</sub>)<sub>n</sub>-R<sub>16</sub>, -S(O)<sub>2</sub>-(CH<sub>2</sub>)<sub>n</sub>-R<sub>16</sub>, -O-(CH<sub>2</sub>)<sub>n</sub>-R<sub>16</sub>, or -N(R<sub>18</sub>)-(CH<sub>2</sub>)<sub>n</sub>-R<sub>16</sub>

wherein n is 0, 1 or 2;

R<sub>16</sub> is selected from halogen, -CN, -NO<sub>2</sub>, -CF<sub>3</sub>, -OCF<sub>3</sub>, -OH, -S-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, -S(O)-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, -S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, -NH<sub>2</sub>, -NH-(C<sub>1</sub>-C<sub>4</sub>)-alkyl, -N((C<sub>1</sub>-C<sub>4</sub>)-alkyl)<sub>2</sub>, COOH, C(O)-O-(C<sub>1</sub>-C<sub>4</sub>)-alkyl or O-(C<sub>1</sub>-C<sub>4</sub>)-alkyl; and

each R<sub>15</sub> is independently selected from -OR<sub>17</sub>, or -N(R<sub>18</sub>)<sub>2</sub>;

R<sub>17</sub> is selected from hydrogen, -(C<sub>1</sub>-C<sub>6</sub>)-straight alkyl, -(C<sub>1</sub>-C<sub>6</sub>)-straight alkyl-Ar, -C(O)-(C<sub>1</sub>-C<sub>6</sub>)-straight or branched alkyl, -C(O)-Ar, or -(C<sub>1</sub>-C<sub>6</sub>)-straight alkyl-CN; and

each R<sub>18</sub> is independently selected from -(C<sub>1</sub>-C<sub>6</sub>)-straight or branched alkyl, -(C<sub>1</sub>-C<sub>6</sub>)-straight or branched alkyl-Ar, -(C<sub>1</sub>-C<sub>6</sub>)-straight alkyl-CN, -(C<sub>1</sub>-C<sub>6</sub>)-straight alkyl-OH, -(C<sub>1</sub>-C<sub>6</sub>)-straight alkyl-OR<sub>17</sub>, -C(O)-(C<sub>1</sub>-C<sub>6</sub>)-straight or branched alkyl, -C(O)-Ar, -S(O)<sub>2</sub>-(C<sub>1</sub>-C<sub>6</sub>)-straight or branched alkyl, or -S(O)<sub>2</sub>-Ar; wherein

any alkyl, alkenyl or alkynyl group is optionally substituted with 1 to 3 independently selected halo groups; and

any Ar, aromatic carbocyclic ring or heterocyclic ring is optionally substituted with 1 to 3 substituents independently selected from halo, hydroxy, nitro, cyano, amino, (C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl, O-(C<sub>1</sub>-C<sub>4</sub>)-straight or branched alkyl, (C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl, or O-(C<sub>2</sub>-C<sub>4</sub>)-straight or branched alkenyl or alkynyl;

any Ar, aromatic carbocyclic ring or heterocyclic ring is optionally benzofused; with the provisos that:

at least two of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, or R<sub>5</sub> is hydrogen;

no more than two of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, or R<sub>5</sub> comprises Ar;

at least two of R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> or R<sub>11</sub> is hydrogen; and

no more than two of R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> or R<sub>11</sub> comprises Ar;

when X is -C(O)-N(R<sub>6</sub>) or -N(R<sub>6</sub>)-C(O)-, then

~~two adjacent groups selected from either R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub>, or from R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub> and R<sub>11</sub>, may not be taken together with the carbon atoms to which they are bound to form a 6-membered aromatic carbocyclic ring; and~~

b) a pharmaceutically acceptable carrier, adjuvant or vehicle.

20. (currently amended): The composition according to claim 19, further comprising ~~of this invention comprise a compound~~ an additional agent selected from an

immunosuppressant, an anti-cancer agent, an anti-viral agent, anti-inflammatory agent, antifungal agent, antibiotic, or an anti-vascular hyperproliferation compound.

21. (original): A method of treating or preventing an IMPDH-mediated disease or condition in a mammal comprising the step of administering to said mammal a composition according to claim 19 or 20.

22. (currently amended): The method according to claim 21, wherein said IMPDH-mediated disease or condition is selected from transplant rejection, graft versus host disease, or an autoimmune disease.

23. (original): The method according to claim 22, wherein said mammal is administered an additional immunosuppressant in a separate dosage form or as part of said composition.

24. (currently amended): A method for inhibiting ~~viral~~ replication of a virus in a mammal comprising the step of administering to said mammal a composition according to claim 19 or 20.

25. (currently amended): The method according to claim 24, wherein ~~the viral replication to be inhibited is that of a~~ said virus is selected from orthomyxovirus, paramyxovirus, herpesvirus, retrovirus, flavivirus, pestivirus, hepatotropic virus, bunyavirus, Hantaan virus, Caraparu virus, human papilloma virus, encephalitis virus, arena virus, reovirus, vesicular stomatitis virus, rhinovirus, enterovirus, Lassa fever virus, togavirus, poxvirus, adenovirus, rubiola, or rubella ~~is inhibited~~.

26. (original): The method according to claim 25, wherein said mammal is administered an additional anti-viral agent in a separate dosage form or as part of said composition.

27. (original): A method for inhibiting vascular cellular hyperproliferation in a mammal comprising the step of administering to said mammal a composition according to claim 19 or 20.

28. (original): The method according to claim 27, wherein said method is useful in treating or preventing restenosis, stenosis, arteriosclerosis or other hyperproliferative vascular disease.

29. (original): The method according to claim 28, wherein said mammal is administered an additional anti-vascular hyperproliferative agent in a separate dosage form or as part of said composition.

30. (original): A method for inhibiting tumors and cancer in a mammal comprising the step of administering to said mammal a composition according to claim 19 or 20.

31. (original): The method according to claim 30, wherein said medicament is useful to treat or prevent lymphoma, leukemia and other forms of cancer.

32. (original): The method according to claim 31, wherein said mammal is administered an additional anti-tumor or anti-cancer agent in a separate dosage form or as part of said composition.

33. (original): A method for inhibiting inflammation or an inflammatory disease in a mammal comprising the step of administering to said mammal a composition according to claim 19 or 20.

34. (original): The method according to claim 33, wherein said method is useful for treating or preventing osteoarthritis, acute pancreatitis, chronic pancreatitis, asthma or adult respiratory distress syndrome.

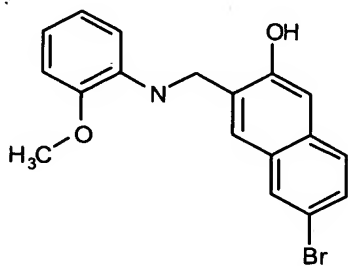
35. (original): The method according to claim 33, wherein said mammal is administered an additional anti-inflammatory agent in a separate dosage form or as part of said composition.

36. (currently amended): The ~~compound of claim 1 or the composition of claim 19 or 20,~~ wherein X is  $-N(R_6)-C(O)-Y-$ .

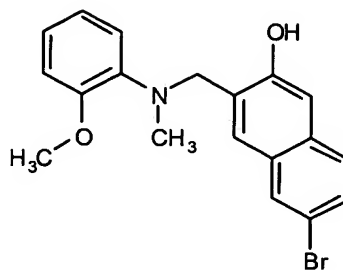
37. (original): The compound or composition of claim 36, wherein Y is  $-C(R_{12})=C(R_{12})-$ .

38. (currently amended): The ~~compound of claim 1 or the composition of claim 19 or 20,~~ wherein Q is  $-N(H)-C(O)-O-$ .

39. (new): A compound selected from the group consisting of **115** and **151**.



**115**



**151**

40. (new): A compound selected from the group consisting of **101, 103, 104, 105, 106, 107, 110, 111, 112, 113, 114, 116, 117, 118, 119, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 148, 149, 153, 154, 155, 156, 159, 160, 162, 163, 164, 165, 166, 168, 169, 172, 173, 175, 177, 178, 179, 181, 182, 183, 184, 185, 188, 191, 192, 193** and **304**.